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BIOMETRICS

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THE BIOMETRICS SECTION, AMERICAN STATISTICAL ASSOCIATION

On The New Biometrics Bulletin

When the American Statistical Association was founded more than a hundred years ago, statisticians were primarily concerned with the collection of data of interest to the State. Within the last sixty or eighty years, however, statisticians have developed methods that have entered one branch of science and industry after another and have attained a central position in biology, physics, chemistry, meteorology, and astronomy, as well as in the social and economic sciences and in mass production and distribution.

The American Statistical Association has not adequately fulfilled its responsibility with respect to this development although its purpose is stated in part "to foster contacts among persons seriously concerned with statistical information, problems, and methods, . . . and to encourage the application of statistical science to practical affairs."

The formation of the Biometrics Section within the American Statistical Association in 1938 marked an important step toward correcting this situation. This step recognized and gave support to the work of biometricians, who since the time of Galton have made important contributions to the subject matter of their own field and have done much to develop the modern statistical method that is of equal importance in many other fields.

The launching of the Biometrics Bulletin is a logical step not only in fostering contacts between biologists concerned with statistical information, problems, and methods but also in stimulating research and in elevating the standards of statistical work that should prove helpful in developing the profession of statistics.

Walter A. Shewhart, *President.*
American Statistical Association.

Biologists and Biometricians

With this first issue of the BIOMETRICS BULLETIN, the Biometrics Section addresses a larger audience than in the past. Biologists and biometricians form a constructive symbiotic pair and the Section is primarily concerned with furthering this relation. Many of our members are now absent on war assignments and we have few opportunities to interchange ideas at national meetings. Under these conditions the BIOMETRICS BULLETIN will be invaluable as a means of communication and as a medium for bringing our biological friends into a coherent organization. The high calibre of our Editorial Committee insures a publication which the biologist can trust. We are especially fortunate in having as the Chairman of our Editorial Committee, Professor Gertrude M. Cox, Director of the Institute of Statistics at North Carolina State College.

C. I. Bliss, *Chairman,*
Biometrics Section.

THE NEW BIOMETRICS BULLETIN

The BIOMETRICS BULLETIN, official organ of the Biometrics Section of the American Statistical Association, is designed primarily for biologists who see in statistics a potent tool for their work. American biologists are realizing that optimum efficiency in research often requires the use of statistics.

The Biometrics Section was established in 1938 to stimulate development of biometrics within the American Statistical Association. From the start the Section has invited biologists to bring new biometrical problems before the membership. Limited at first to meetings with the parent Association, attendance was primarily biological statisticians.

As American biologists have become increasingly dependent upon statistical methods, however, the Section has expanded its program to reach more of the present and potential users of statistics in the biological sciences. Since 1941 special programs have been arranged at meetings of the Federation of American Societies for Experimental Biology, of the American Society of Agronomy, of the American Association of Cereal Chemists and of the American Association for the Advancement of Science.

Biometricians interested in the broader development of statistics were invited to join the American Statistical Association; many have joined.

There still remains a large group outside the Section who receive notices of all meetings. The first issue of the BIOMETRICS BULLETIN is being sent to everyone in this group. The editors hope that this publication will serve to draw the professional biometricians—the nucleus of the Section—and the biological research workers into closer accord.

There are two types of membership, Members and Associate Members. Any Member of the American Statistical Association may subscribe to the BIOMETRICS BULLETIN at the rate of $1.00 and will be enrolled as a Member of the Biometrics Section. Membership in the American Statistical Association is open to anyone interested in statistics and at the regular rate of $5.00 per year includes the Journal of the Association, which publishes many articles of interest to biometricians, and the Bulletin of the Association. Membership in the American Statistical Association and the Biometrics Section at a total of $6.00 per year will appeal to biologists who are actively interested in statistical methods. Those interested only in the Biometrics Section are cordially invited to become Associate Members. Associate membership at $2.00 a year includes the BIOMETRICS BULLETIN and all privileges of Section membership except that of holding office. It is our hope that the BIOMETRICS BULLETIN will be so valuable that biologists who make even occasional use of statistical method will be unwilling to get along without it.

The BIOMETRICS BULLETIN will be developed to meet the needs of the membership. Many features have been planned primarily for the novice. There will be a column of Queries to which members are invited to submit questions which can be answered briefly. If you have a statistical question which has been troubling you, here is a chance to have it answered authoritatively. Larger problems will be covered by short expository articles written on invitation by qualified professional biometricians. Review articles will highlight the applications of statistics in substantive fields such as ecology, entomology, forestry, plant breeding, bacteriology and many others. The first of these, on uses of statistics in medicine, appears in this issue. Although few of the papers read at the meetings of the Section can be published in full in the BULLETIN, abstracts of them, usually in advance of their final publication will appear.

The Section will continue to hold joint meetings with biological as well as with statistical societies. The BIOMETRICS BULLETIN will carry notices of these programs. News items in the BULLETIN will enable the reader to follow the activities of the members as well as topics of biometric interest. Short articles will report on American educational institutions which offer courses or conferences on biometrics, both at the amateur and at the professional level. Many professional biometricians have been drawn actively into war projects. As soon as the war contributions of this group can be reported, they will be noted in the BULLETIN.

Through the BIOMETRICS BULLETIN we want to lay the groundwork for a full-fledged biometrical journal at the end of the war. Meanwhile the greater your cooperation and the larger our membership, the bigger and better we can make the BULLETIN. The enclosed application form is for your convenience in joining the Section either as Member or as an Associate Member. We welcome your suggestions of features you would like in the BULLETIN or at our meetings, also news items and queries. Will you send us the names of any friends who should receive this first issue of the BIOMETRICS BULLETIN? A later issue will list the membership of the Biometrics Section.

SOME USES OF STATISTICAL METHODS IN MEDICINE

JOHN R. MINER, Sc.D.
Division of Publications, Mayo Clinic—Rochester, Minnesota

Since medicine deals with living organisms, which in Yule's phrase are "affected to a marked extent by a multiplicity of causes," it is natural that statistical methods are often useful in the elucidation of medical problems. This is true, not only of such basic medical sciences as physiology, but of clinical investigations of problems of etiology, diagnosis and prognosis as well as the evaluation of the effectiveness of different methods of treatment.

An example of the use of statistical methods in investigation of possible etiologic factors is the work of English, Willius and Berkson[1] on tobacco and coronary disease. These authors found that in the age group from forty to forty-nine years the proportion of smokers among men who had coronary sclerosis was significantly greater than among those who did not have it and conversely that the incidence of coronary disease among smokers was greater than among nonsmokers. Furthermore, among smokers its incidence increased with increasing degree of smoking. In discussion of this paper Weiss pointed out that this statistical association between smoking and coronary disease did not necessarily imply causation and English and his associates "presumed that in all probability the smoking of tobacoo was not an etiologic factor but was perhaps an influence that affected the course and progress of the disease."

The work of Matthews and his associates[2] on the Exton-Rose dextrose tolerance test illustrates the use of statistical methods to determine the most efficient criteria for interpretation of a diagnostic laboratory test. In the Exton-Rose procedure a sample of blood is taken just before the patient drinks a solution of dextrose. Thirty minutes later a second sample of blood is taken and a second dose of dextrose is given. Thirty minutes after administration of the second dose of dextrose, that is, an hour after the beginning of the test, a third sample of blood is taken. The criteria that Exton and Rose had proposed, which involved the concentration of sugar in all three samples of blood, agreed with the clinical diagnosis in 88 per cent of the cases of Matthews and his associates. The simpler criterion that, if the concentration of sugar in the one hour sample was 158 mg. per 100 c.c. of blood or more, the patient should be considered diabetic agreed with the clinical diagnosis in 98 per cent of the cases.

An example of the use of statistical methods to determine prognosis is the work of Walters, Gray and Priestly[3] on malignant lesions of the stomach. They found that 29 per cent of patients on whom resection was performed survived for five years or more, whereas the corresponding proportion for those on whom a palliative operation was performed was 1 per cent. The proportion of those who lived five years or more after leaving the hospital was greater among those who did not have metastasis than among those who did and it varied inversely with the grade of malignancy (Broders' method).

Cohn and Lingg[4] have made a statistical study of the natural history of rheumatic cardiac disease. This study differs from most studies of this disease in the fact that the individual patients were observed over long periods, so that the development of rheumatic phenomena was known in continuity. The data, 95 per cent of which were for the white races, were classified by sex, age of patient at onset, type of initial manifestations, duration of disease relation of duration of disease to age

at onset, distribution of cases at various age periods, relation of recurrences of rheumatic activity to age, relation of severity of infection to age at onset and relation of type of onset to subsequent infection. There has been doubt whether the diminution of the rate of recurrence that takes place about the age of puberty is due to this physiologic change or whether it occurs about five years after the first infection because of the development of immune processes. Since the most frequent age of onset is at seven or eight years, five years after onset would be most often in the period of puberty. By classifying their data by age at onset, Cohn and Lingg obtained evidence that it is puberty that influences the frequency of recurrance.

In an attempt to supply evidence bearing on the questions: Will nephrectomy shorten the patient's life? Will it handicap him and limit his work and activities? Kretschmer[5] made a statistical analysis of the results of his examination of 156 patients on whom he had performed nephrectomy. He divided the data on the basis of the lesions for which the operation was performed, and also presented results for the group as a whole. The average length of time between nephrectomy and the examination was eight years and two months. Pain in the remaining kidney occurred in only seven cases. In some of these cases it was due to organic disease rather than to compensatory hypertrophy. Eighteen patients had cardiac involvement. The incidence of cardiac enlargement among the patients more than fifty years of age was about what might be expected among persons of similar age who had not undergone nephrectomy. The weight of most patients remained the same. In fourteen cases the blood pressure increased but the patients in these cases had reached an age at which hypertension might be expected. The results of urinalysis depended on the lesion for which nephrectomy was performed. Elevation of nonprotein nitrogen occurred in 15 per cent of the cases. Seventy-three per cent of the patients were able to pass the Newburgh concentration test. Scoliosis was present in eighteen cases.

In discussion of Kretschmer's paper, Woodruff[6] pointed out that the study did not entirely answer the questions posed at the beginning of the paper. He suggested that it should deal, not only with the living patients, but also with those who had died and the cause of their death.

It has been suggested that the administration of ascorbic acid has a beneficial effect on persons suffering from chronic lead poisoning. With a view to throwing light on this question Evans and his associates[7] tested the concentration of lead in the blood and urine of a group of men working in a plant for the manufacture of tetra-ethyl lead. These concentrations during a year in which these men received 100 mg. of ascorbic acid daily by mouth were compared with the concentrations for the same men during the previous year, in which they did not receive ascorbic acid, and with the concentrations for a control group who did not receive ascorbic acid. As the differences were not statistically significant, Evans and his associates concluded that they had not found any reason for recommending the use of ascorbic acid to minimize the effects of lead absorption.

In a study of toxic reactions among patients who had been given a sulfonamide compound, in most cases for pneumonia, Dowling and Lepper[8] found that 29.4 percent of patients given sulfapyridine had a toxic reaction. The corresponding proportions were 11.8 per cent for sulfathiazole and 7.7 per cent for sulfadiazine.

In an experimental study of prevention of rabies by local treatment of wounds contaminated with rabies virus, the treatment being instituted within thirty minutes, Shaughnessy and Zichis[9] found that only 11 per cent of animals treated with fuming nitric acid and only 6 per cent of those treated with 20 per cent solution of soft soap became infected, as against 63 per cent infected among the untreated controls. Tincture of iodine compared favorably with nitric acid or soap solution when used at an interval of thirty minutes but when used after two hours it was considerably less effective. Packing the wounds with sulfanilamide after they had been treated with soap solution did not seem to decrease the incidence of rabies.

The foregoing are only a small sample of uses to which statistical methods have been put in the solution of medical problems.

See page 5 for footnotes.

THE INSTITUTE OF STATISTICS OF THE UNIVERSITY OF NORTH CAROLINA

The Department of Experimental-Statistics was organized at North Carolina State College in January, 1941. Its functions were to teach courses in applied and in mathematical statistics, to carry on research in statistical methodology and application, to advise on the design of experiments and the analysis of data, and to provide a computational service primarily for the Agricultural Experiment Station. The demand for all of these services increased rapidly, and the work broadened in scope beyond biological into social and industrial research. An increasing number of requests for assistance were received from research agencies, especially from organizations handling southern research projects.

The increased demand for the statistical services of the Department, its broadening scope and the necessity for concurrent research in methodology, led to the organization of the Institute of Statistics. This was approved by the Executive Committee of the Board of Trustees of the University of North Carolina in September, 1944. The General Education Board has appropriated $87,000 to the University of North Carolina toward the support of the Institute during a five-year period, to supplement funds from federal, state and other agencies.

Plans for the Institute of Statistics can be indicated best by describing the work of the Department during its four years of existence.

TEACHING. At present, courses in applied and mathematical statistics are being given to undergraduate and graduate students, faculty, extension workers and special-session groups. These courses will be supplemented by others as new faculty members are secured.

With the present facilities the mathematical statistician is brought into contact with practical biological, social, and industrial problems concurrently with his formal training in theory. This combination provides unlimited opportunities for graduate studies on the solution and testing of mathematical theories of statistics. The applied statisticians are also given a thorough training in mathematical statistics, so that they can appreciate the assumptions and theories underlying the methods of statistics.

The regular courses are supplemented by intensive short courses. Several of these were given during the summer of 1941 with the assistance of Dr. Harold Hotelling, and others are planned when world conditions permit. Shorter work conferences have been held for invited research workers from the southern states. At a Plant Science Work Conference in February, 1944, instruction was supplemented by discussion of the research problems of those in attendance. An Animal Science Work Conference in October, 1944 featured a series of lectures by Professor G. W. Snedecor. This was followed in November, 1944, by an in-

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Footnotes continued from page 4.

1. English, J. P., Willius, F. A., and Berkson, Joseph: Tobacco and coronary disease. J. A. M. A. 115:1327-1329 (Oct. 19) 1940.
2. Matthews, M. W., Magath, T. B. and Berkson, Joseph (with assistance of Gage, R. P.): The one hour-two dose dextrose tolerance test (Exton-Rose procedure): diagnostic significance. J. A. M. A. 113:1531-1537 (Oct. 21) 1939.
3. Walters, Waltman, Gray, H. K. and Priestley, J. T.: Malignant lesions of the stomach; importance of early treatment and end results. J. A. M. A. 117: 1675-1681 (Nov. 15) 1941.
4. Cohn A. E. and Lingg, Claire: The natural history of rheumatic cardiac disease: a statistical study: I. Onset and duration of disease. J. A. M. A. 121:1-8 (Jan. 2); II. Manifestations of rheumatic activity: recurrence, severity of infection and prognosis. 113-117 (Jan. 9) 1943.
5. Kretschmer, H. L.: Life after nephrectomy. J. A. M. A. 121:473-478 (Feb. 13) 1943.
6. Woodruff, S. R.: Discussion. J. A. M. A. 121:478 (Feb. 13) 1943.
7. Evans, E. E., Norwood, W. D., Kehoe, R. A. and Machle, Willard: The effects of ascorbic acid in relation to lead absorption. J. A. M. A. 121:501-504 (Feb. 13) 1943.
8. Dowling, H. F. and Lepper, M. H.: Toxic reactions following therapy with sulfapyridine, sulfathiazole and sulfadiazine. J. A. M. A. 121:1190-1194 (Apr. 10) 1943.
9. Shaughnessy, H. J. and Zichis, Joseph: Prevention of experimental rabies; treatment of wounds contaminated by rabies virus with fuming nitric acid, soap solution, sulfanilamide or tincture of iodine. J. A. M. A. 123:528-533 (Oct. 30) 1943.

tensive course in Quality Control. A nutrition group will be brought together late this spring. These conferences are planned to provide for better designed experiments which will lead to more conclusive results from research projects. Funds have been provided for a series of such conferences. It is planned that an opportunity will be provided for these groups to return for further consultation and assistance every two or three years.

CONSULTING. The faculty assists local and other research workers in the South with the planning of their experiments, the selection of appropriate statistical techniques for the analysis of their data and the interpretation of the results. Many individual scientists from various states and foreign countries have applied for aid from staff members on special problems relating to their work. During the period of three and one-half years prior to July 1, 1944, nearly 500 different individuals wrote letters asking staff members for statistical assistance. Of these, 78 percent were from states east of the Mississippi River and 37 percent were from the southern states. During the same period more than 200 out-of-town visitors, representing different federal agencies, experiment stations, universities and other organizations, inspected the facilities of the Laboratory or asked for help with specific research problems. They came from 43 states and 9 foreign countries. This list has increased considerably during the past eight months.

In addition to this type of consultation, the staff members visit other institutions and research organizations to advise on the design of experiments and the analysis of experimental data. Thus the consulting statisticians of the Department have had the benefit of first-hand observation regarding many southern research projects.

RESEARCH. Research in statistical method ology is planned to develop and test procedures for various specialized fields of investigation. These have included hundreds of designs for agricultural sampling projects and for field, greenhouse and laboratory experiments concerning forest grazing, control of insect pests, crop yields, human nutrition, medical research, vitamin needs and food qualities, and chemical, physical and production experiments. Many staff members have had professional training for research in one or more of these specific fields as well as a background in statistical method.

It has been demonstrated that the new designs enabled the experimenters to obtain more accurate results with a smaller expenditure of money. These savings have impressed research directors with the value of statistics and have aided materially in the expansion of statistical work.

The Department cooperates directly, or through its relationships with other departments on the campus, with many federal, state, and private research organizations. Among them are the Bureau of Agricultural Economics, Weather Bureau, Soil Conservation Service, Bureau of Plant Industry, Farm Security Administration, Bureau of Mines, Agricultural Adjustment Agency, Tennessee Valley Authority and Southern Cooperative Group. From the beginning, the North Carolina Research Office of the Division of Agricultural Statistics, Bureau of Agricultural Economics, has formed an integral part of the existing Laboratory with Walter A. Hendricks in charge of the work and Glen F. Vogel assisting him.

SERVICE. As a regular service the Laboratory analyzes data gathered by workers in the North Carolina Experiment Station and cooperating agencies. Consultations with outside research workers often require similar assistance on the computations. Many manuscripts are reviewed in their statsitical aspects, not only for local investigators but also for outside workers and journal editors.

FACULTY. In addition to Mr. Hendricks and Mr. Vogel the faculty now includes Gertrude M. Cox, Director of the Institute of Statistics and Head of the Department of Experimental Statistics, J. A. Rigney, R. E. Comstock, J. M. Clarkson, R. L. Anderson, and R. J. Monroe, Associate and Assistant Professors; and Margaret Fleming, Sarah Porter, Ann Castleman and Virginia Montague, Technical Assistants.

Directly Observable Genetic Changes in Population of Drosophila Pseudoobscura

TH. DOBZHANSKY
Columbia University

Summary of a paper read before the Section in Washington, D.C., Dec. 29, 1944

Evolutionary changes in natural populations are in general too slow to be observed directly; the evidence for evolution is for the most part inferential. Only in some exceptionally favorable cases can evolutionary changes be actually witnessed. One such case is that of the fly species *Drosophila pseudoobscura.* Natural populations of this species on Mount San Jacinto, Calif., have three different gene arrangements commonly encountered in their third chromosomes. These gene arrangements are designated as ST (=Standard), AR (=Arrowhead), and CH (=Chiricagua). Frequent samplings of the populations during four years (1938-1941) disclosed that the relative frequencies of the gene arrangements in them change from month to month. Furthermore, the changes are cyclic, apparently following the annual climatic cycle. ST is most frequent in winter and in early spring (March), and least frequent in early summer (June). The cycle of CH is the reverse of that of ST. The frequency of AR changes relatively little.

The changes are caused by inequalities of the adaptive values of the three kinds of chromosomes: ST chromosomes are relatively unfavorable, and CH chromosomes relatively favorable, in late spring and early summer. Natural selection modifies the composition of the populations accordingly. The frequencies of each chromosome type are waxing or waning during seasons when the respective types are relatively more or less favorable for the survival of their carriers.

This explanation of the changes necessitates the assumption that the adaptive values of the three gene arrangements differ very greatly. Thus, in one of the localities the frequency of CH is almost doubled within a time interval which corresponds to hardly more than three fly generations. Selection coefficients that are necessary to bring about so rapid a change are of a different order of magnitude from those customarily assumed to be effective in bringing about evolutionary changes in nature. It is tempting to suppose that the changes observed are caused not by natural selection but by some other factor, such as periodic invasion of the localities studied by flies from other localities differing in the relative frequencies of these gene arrangements. Brief consideration will show this alternative explanation to be invalid. Assume, for the sake of argument, that the frequencies of the chromosome types in a certain locality change at a certain season because of an invasion from another locality. The changes observed are, however, cyclic. To bring the relative frequencies of the gene arrangements back to the original values it is necessary that the chromosomes of the invaders be discriminated against by a process of naural selection to an extent sufficient to eliminate them. The assumption of invasions is unnecessary.

The speed of dispersal of the flies has been studied experimentally by Wright and Dobzhansky. In a reasonably uniform two-dimensional medium the flies move approximately at random. The distance between the points at which an average fly finds itself on successive days depends upon the temperature of the environment. At temperatures normally prevailing in summer at mid-altitudes in the mountains of southern California this distance varies roughly from 50 to 150 meters. Since, however, the movements are at random, the offspring of a fly will be found mostly within less than a kilometer from the point where that fly was born. Studies on mutant genes harbored in natural populations have shown quite unambiguously that populations found at a given collecting station in different months are more similar genetically than populations of collecting stations one half to several kilometers apart sampled simultaneously. This shows that large scale migrations and population invasions do not, as a rule, take place.

Laboratory experiments now in progress have produced conclusive evidence of the inequalities of the adaptive values of the chromosomes with the different gene arrangements

found in the populations of Mount San Jacinto. Artificial populations have been set in "boxes" the construction of which represents a modification of the system proposed by L'Héritier and Teissier. A group of flies containing a known mixture of the chromosomal types is introduced into the box; fresh food is supplied and the worked-out food removed at desired intervals. From time to time a sample of the eggs deposited in the box is taken, and the chromosomes analyzed in the larvae which develop from these eggs. Experiments conducted at temperatures of 21° C or higher have invariably produced perceptible, often, rapid, alterations in the composition of the populations. In mixtures containing ST, AR, and CH chromosomes the frequencies of ST increase while those of AR, and especially of CH, decrease. This is analogous to the changes observed in nature during the summer months. In mixtures containing ST and AR, or ST and CH, the frequencies of ST increase at the expense of AR and CH; in mixtures of AR and CH the frequency of AR increases. Thus far the reciprocal changes (analogous to those taking place in nature during spring) have not been reproduced in the "boxes". At a temperature of 16½° C the course of events in the "boxes" is, however, different from that observed at higher temperatures, namely, the relative frequencies of the different chromosome types remain unchanged.

QUERIES

Biologists ask many questions about statistics, ranging from the design of experiments all the way down to mistakes in computation. Some wish information about theory, others about calculational procedures, and still others (and this is perhaps the largest group) about interpretation of statistical results. This department is intended to be helpful along the whole array of difficulties.

The help will be mutual. We hope the inquirer will profit by the exchange, but we know the statistician will. He can learn about diverse applications of his theory, about holes that need to be plugged with research and about lapses in his presentation of his subject to the consumer. The reader should not be bashful in sending in his problems: he is not wasting anybody's time but rather is adding to the fund of common knowledge. The success of this venture depends upon his participation.

The effort will be made to include a graded list of answers in each issue of the Bulletin. As soon as a stock of "Queries" is accumulated, they can be sorted into groups, each involving both elementary and advanced treatment. Insofar as possible, answers which are not of general interest will be sent directly to the inquirer.

Controversial questions are not excluded and, within the limitations of available space, discussion and criticism will be published. If this becomes too extensive, or if questions require more complicated answers, they may be treated as expository articles.

If this program meets your approval, send your questions. If not let us have your suggestions. Address "Queries, Statistical Laboratory, Iowa State College, Ames, Iowa".

Query

We are told that a non-significant result does not mean that the null hypothesis is true. What sort of conclusions can be drawn from a non-significant result?

Answer.

While we cannot infer that the null hypothesis is true, it is possible to draw conclusions which, although much weaker, nevertheless are useful in deciding future action. These conclusions are obtained by the construction of confidence limits.

To illustrate, suppose that the observed difference between two treatment means is 1.0, with an estimated standard error of 1.5, based on 20 degrees of freedom. If d is the real difference between the treatments, it is known that the quantity

$$(1.0\text{-}d)\,/1.5$$

is distributed as Student's t with 20 degrees of freedom. The five percent level of this t is 2.09. Consequently, the quantity above will lie inside the limits plus and minus 2.09, unless a 1 in 20 chance has occured. This result implies that d lies between 1.0 plus and minus (1.5×2.09), that is, between -2.1 and 4.1, apart from the 1 in 20 chance.

Thus, in place of the unwarranted conclusion: "there is no real difference," we substitute the conclusion: "it is reasonably certain that

the real difference lies inside the limits −2.1, 4.1". Further, we can select the degree of certainty that is attached to this statement.

After examination of the limits, −2.1, 4.1, the research worker may conclude that even if d lies at one of these limits he will commit no serious error in assuming that d is zero in his future work. In this case the experiment has established the result that d is *zero for all practical purposes*, except for the possibility that the 1 in 20 chance has occurred. On the other hand, it may be that future action taken on the assumption that d is zero will be unwise should d differ from zero by as much as −2.1 or 4.1. In this event the proper verdict is that further experimentation is needed to establish the value of d within narrower confidence limits.

Two complications may arise. The first is mathematical and occurs when the null hypothesis is rather complex. For instance, if the null hypothesis states that the real relation between y and x is a straight line, it may not be clear how to put limits on the degree of curvilinearity that might exist in the relationship. In such cases a mathematical statistician should be consulted. The second complication is illustrated by the case in which the real difference between two treatments is known to vary with the conditions of the experiment, as is common, for instance, in field experimentation. Here a conclusion of the above type from a single experiment may have no validity for other experiments or for the population to which the conclusions are to be applied. What is needed is a series of experiments which *are* a representative sample from this population. Given such data, the technique will apply, though the mathematics is likely to be more complicated than in the simple example of the t-test.

W. G. Cochran,
Iowa State College

NEWS AND NOTES

There were two sessions of the Biometrics Section at the annual meeting of the American Statistical Association in Washington, D. C., on December 27 to 29, 1944. The papers read at these sessions will be abstracted in the Bulletin. A number of papers of interest to biometricians were read at other sessions of the meetings. Among these were two reports on the "Master Sample of Agriculture". The first, on "Development and Use", was given by A. J. King, Bureau of Agricultural Economics and Resident Collaborator of the Statistical Laboratory at Ames, and the second, on "Design", by R. J. Jessen, Bureau of Agricultural Economics. Gertrude M. Cox, North Carolina State College, appraised the "Opportunities for Teaching and Research" in a symposium on job opportunities in statistical work. The converse of this picture was described by W. G. Cochran, Iowa State College, in his discussion of "Training for Statistical Work in Agriculture and Biology". Two papers dealt with the application of the Shewhart quality control chart to problems of biological interest. One of these was by Lila F. Knudsen, Food and Drug Administration, on "Control Chart Analysis of Penicillin Assays". The second by Sophie Marcuse, Bureau of Human Nutrition and Home Economics, concerned "Quality Control as Applied to the Testing and Marketing of Foods."

W. G. Cochran, Professor of Mathematics and Research Professor in the Statistical Laboratory, Iowa State College, has returned to Ames after a year's leave of absence at Princeton University on a Navy project. While in the East, he spoke at a meeting of the Connecticut Chapter of the American Statistical Association at Yale University on December 7, 1944. His subject was "Statistical Contributions of Student", with particular reference to the design of experiments.

The Animal Vitamin Research Council has recently appointed a Statistical Committee with the following membership: C. I. Bliss, chairman, B. L. Oser, K. Morgareidge and G. H. Kennedy. The Committee is to be available for consultation regarding the planning and interpretation of the collaborative experiments undertaken by members of the Animal Vitamin Research Council.

W. T. Federer, Agricultural Statistician, Bureau of Agricultural Economics, USDA, has recently joined the staff of the Statistical Laboratory at Iowa State College as Collaborator, to work in the field of experimental design. He came to Ames from Salinas, California where he has been working on the special Guayule Research Project, Bureau of Plant Industry, USDA.

The course at Yale University, Pharmacology 111, on biometrics as applied to biological assay will be open this year to qualified persons outside the University. In order to accommodate research workers who may wish to commute, the class will meet one afternoon each week for the period from February to June. Further information can be had by application to the Department of Pharmacology, Yale University, New Haven, Conn.

ABSTRACTS

This section will include abstracts of papers in programs sponsored by the Biometrics Section. All abstracts are prepared by the author from the paper as prepared for publication if different from the paper as read. If publication references are not given with the abstracts they will be printed with the original abstract numbers as they become available.

Papers read at Cleveland, Ohio, September 11, 1944:

1. SHERWOOD, M. B. and E. J. de BEER (The Wellcome Research Laboratories) **The Paper-disc, Agar-plate Method for the Assay of Antibiotic Substances.**

Statistical principles of experimentation were applied in a study of factors influencing the assay of penicillin by the paper-disc modification of the Oxford plate method.

Dosages were spaced at equal logarithmic intervals so that orthogonal coefficients and the analysis of variance could be used in studying the dose-response curve. Practically all of the variance was due to the linear term and the diameter of the zone of inhibition was a linear function of the log-concentration of penicillin.

Zones of inhibition decreased as agar thickness increased; the displacement in the dose-response curve was significant. With comparatively thick or thin agar, curvature as measured by the quadratic and cubic terms became significant although the greater part of the variance was still due to the linear term.

The number of test organisms likewise affected the assay. Smaller quantities of inoculum gave significantly larger zones of inhibition and increased the slope. This did not lead to greater precision since the standard deviation increased simultaneously so that the ratio of the standard deviation to the slope was approximately the same for all inoculum levels studied.

An extensive analysis of test assays was also made.

2. MILLER, LLOYD C., (Winthrop Chemical Co.) **Studies on the Biological Assay of Penicillin.**

Penicillin samples are assayed by comparing their effect upon bacterial growth on an agar plate with the effect produced by a reference standard. A 2 x 2 factorial design was used with two samples each of two concentrations of both standard and unknown on each plate. Four such plates constitute a unit assay, and several assays, agreeing with each other within the error of estimate, are run on each lot before release. The relative potency, its standard error, the standard deviation of a single response, and the slope of the composite dosage-response curve are readily computed by the method of Bliss (J.A.S.A. *39*, 479 (1944)). The standard deviation and slope were plotted against the date on a quality control chart, which showed that the early experience with the method was marked by instability of slope and standard deviation. Later both became stabilized except for two periods when the assay had to be left in inexperienced hands. The chi-square test for variance confirmed these observations

Although the inherent precision of the penicillin assay was found to be considerably better than that of most other biological assays, the very unstable nature of penicillin raises objections to accepting this estimate of precision. Therefore the quality control chart is especially useful in providing the assayist with an immediate comparison of each day's assay with past experience.

3. BLISS, C. I. and B. L. BARTELS (Yale University). **The Use of Past Exerience in the Biological Assay of Digitalis.**

This analysis of the variation in the lethal dose of U.S.P. Digitalis Reference Standard (1942) to cats in twelve laboratories supplements an earlier report on the U.S.P. collaborative digitalis assays (J. Amer. Pharm. Assoc., Scient. Ed. 33: 225-245; 1944). The U.S.P. assay requires that the dose of standard must be determined within fifteen days of that for the unknown. It depends statistically upon the mean and the standard deviation. At present these are determined from the data of the individual assay. If they were sufficiently stable that past experience could be utilized in evaluating current results, the efficiency of the assay could be increased. Using as the unit the logarithm of the individual lethal dose for more than 2200 cats, the stability of the mean and standard deviation was examined for varying periods of time within each laboratory. The mean log-dose differed significantly between laboratories and showed trends within laboratories when tested by control chart techniques coupled with the analysis of variance. In ten of the twelve laboratories the standard deviation showed good stability within and between laboratories. The stability in the standard deviation and to a limited extent in the mean are favorable toward the utilization of past experience in the digitalis assay. Aberrant individuals falling outside the expected range of variation numbered only sixteen and always died from too small a dose. Rules for identifying and excluding them are proposed. Analysis showed that cats as small as 1.5 kg. could be used effectively for assaying digitalis.

4. **SNEDECOR, GEORGE W. and W. R. BRENEMAN,** (Iowa State College), **A Factorial Experiment to Learn the Effects of 4 Androgens Injected into Male Chicks.** (Iowa State College Journal of Science, Vol. 19, No. 3, April 1945).

A 2^4 factorial experiment was set up to study the interactions among the effects of four sex hormones on the comb and testes of male chicks. From statistical interactions it was hoped to make some inferences about the interactions of these androgens in the body of the chick. Each of the 16 treatments was applied to from 10 to 13 chicks housed together. The treatments received by lots of chicks were indicated by head stains. This prevented the confounding of treatment and environmental effects always possible when lots are kept in separate cages.

It was found that in this experiment the disproportion among the subclass numbers caused no appreciable decrease in efficiency even when evidence of interaction was lacking. Hence, the unweighted group means were used throughout the factorial analysis.

On account of heterogeneity in both variance and regression, the logarithm transformation was used, but it affected the results very little. Although the body weights of the lots differed significantly ($P=0.02$), they were not associated with treatment or with treatment effects. Hence, lot means of comb and gonad weights were adjusted for regression on body weight.

In the gonad series, the regressions of log. gonad weight on body weight were homogeneous. In testing the significance of effects, the correction due to Yates was applied to the mean square if the probability was near 0.05. In each case the correction was beyond the number of significant digits being carried. Heterogeneous regressions were encountered in the log. comb series, hence adjustments to mean body weight were made by use of individual lot regressions. Neglect of the variances of the regression coefficents produced a bias of 1.6 percent in the error for main effects; but since no conclusions were affected, the more acurate computation of error was ignored in testing the various partial effects.

Only one of the 15 main effects and interactions was informative. The data required the kind of detailed analysis explained by Yates on pages 9-13 of his "The design and analysis of factorial experiments."

5. **NORTON, H. W.,** (U. S. Weather Bureau), **Calculation of Chi-Square for Complex Contingency Tables.**

Bartlett generalized the treatment of the 2 x 2 of fourfold contingency table, showing explicitly how to handle the 2 x 2 x 2 table, which results when data may be independently divided into two parts in three distinct ways, e. g., by sex, by treatment, and by mortality. The extension of the method to the 2 x 2 x 2 x . . x 2 table was obvious, and it was indicated how the 2 x 2 x 3 table could be discussed, the general method requiring the solution of simultaneous non-linear equations. The present paper derives and exemplifies a convenient procedure of successive approximation for solving the R-1 simultaneous non-linear equations which yield the departures from homogeneity in a 2 x 2 x . . . x 2 x R table. The example uses data in a 2 x 2 x 12 table, and includes the use of the departures to find the expected values and to calculate chi-square.

Papers read at Wahington, D. C., December 29, 1944.

6. **EMLEN, J. T., Jr.** (John Hopkins University), **Measurement of Urban Rat Populations.**

Rat populations in 89 city blocks in Baltimore, Maryland were measured by means of exhaustive trapping campaigns. About ninety percent of a block's population were usually caught in to to three weeks of continuous trapping. Immigration and population drift were found to be of slight consequence, as indicated by very large differences between adjacent blocks and by the success of exhaustive trapping in blocks adjacent to heavily infested areas. The curve of catch size on successive nights resembled a geometric progression but gradually leveled out as trap-shy rats became relatively more numerous. The size of the catch on any particular night near the start of a campaign was roughly proportional to the population present at that time at trap densities between 0.6 and 3.0 traps per rat.

7. **POPE, O. A.** (USDA Bureau of Plant Industry). **Some practical Problems in the Use of Modern Experimental Designs.**

Any research worker operates within certain limitations of facilities, but in addition the biologist frequently must deal with physiological or other peculiarities inherent in the material being studied. Consequently, the choice of a design for an agricultural experiment usually requires a consideration not only of theoretical efficiencies but of any biological peculiarities that may affect the results. Simplicity of structure and a high theoretical efficiency are considerations of major importance, but the design chosen should also provide for salvaging a large amount of information if common hazards invalidate a portion of the data. Examples used illustrate the basis for choice among certain types of lattice and factorial designs.

8. **DUNN, HALBERT L., M.D.** (U. S. Bureau of the Census). **The Effect of War on Where People Live.**

A brief history of census inquiries in connection with State of birth and the use of such information in connection with the description

of movement of native population within the Unitd States is reviewed. The *10 Percent Mortality Sample* and a preliminary tabulation of this sample for two months according to State of birth is then described. There is a discussion of significant changes between the State-of-birth picture for the native population as given by the tabulation from death certificates in contrast to the 1940 State-of-birth tabulations from census figures. After a brief discussion on possible causes of internal population movement within the last four years, it is suggested that the next population census might furnish an opportunity to study the significance of State-of-birth data coming from death certificates and from population enumeration. The author suggests that if such a bridge between the two sets of data could be produced in 1950, State-of-birth tabulations from death certificate information might give a measure of internal migration in the decade following 1950.

9. WADLEY, F. M., (Bureau of Entomology and Plant Quarantine). **Some Trials of Incomlete Block Experimental Designs in Insect Population Problems.**

The various incomplete block designs are adapted where large numbers of treatments are to be compared in plot tests. If the small blocks are really different, the plans will show a gain in efficiency. It may well be asked if they offer possibilities in insect population problems.

Three experiments are cited. A triple lattice test on barley varieties, with three replications of 100 varieties, as to resistance to "green bugs", showed a 20 percent gain in efficiency over randomized complete blocks. A simple lattice test with four replications of 49 corn strains, for resistance to corn borer met with many experimental difficulties and showed no special gain. A lattice square experiment on cotton, with five replications of 16 insecticidal treatments, showed gains of 15 percent to 50 percent in aphid and boll weevil population studies.

It appears that these designs offer promise in insect studies where the number of experimental treatments is large.

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